IN THE CLAIMS

C1

5. (TWICE AMENDED) The composition of claim 4, wherein the apoprotein polypeptide is as shown in SEQ ID NO:9.

C2

33. (NEW) The composition of claim 1, wherein the apoprotein polypeptide comprises from about 350 to about 400 amino acids. need base sequence

IN THE SPECIFICATION

At page 1, beginning at line 1, please replace the paragraph with the following:

C3

CROSS-REFENCE TO RELATED APPLICATIONS

This is related and claims priority to USSN 08/904,871, filed August 1, 1997, now issued as U.S. Patent No. 6,046,014, (also published as WO 98/04700), and USSN 60/023,217, filed on August 2, 1996, both of which are incorporated herein by reference for all purposes.

REMARKS

Claims 1-32 are currently pending in the application. In the current Office Action, claims 5 and 8 were objected to for alleged informalities. Claims 1-32 were rejected under 35 U.S.C. §112 first paragraph as allegedly lacking enablement for a composition comprising an apoprotein comprising between about 190 and about 400 amino acids. Claims 1-32 were also rejected under 35 U.S.C. §112 first paragraph as allegedly lacking proper written description. Claims 1-3, 6-7, 9-22, 25 and 27-32 were rejected under 35 U.S.C. §102(b) as being anticipated by WO 98/05944. Such claims were also rejected under 35 U.S.C. §102(e) as being anticipated by U.S. Patent 6,046,014. The specification and Claim 5 are amended herein.

Specifically, claim 5 is amended as per the Examiner's helpful suggestion to correct a typographical error. New Claim 33 is also added herein. Support for such can be found in many places within the specification as filed, e.g., page 8, lines 9-15. Also, the specification is amended to more clearly show the priority and to update a related application in the priority claim. A request for Corrected filing Receipt is also filed herewith.

Applicants respond to these objections and rejections as noted below. Additionally, Applicants respectfully traverse each of the rejections for the reasons noted below.

No new material has been added through any of these changes and Applicants respectfully request entry of the amendments.

Objections to the Claims

Claims 5 and 8 were objected to in the present Office Action. Claim 5 was objected to for a typographical error which is corrected with the amendment herein (i.e., "aopprotein" is corrected to read "apoprotein").

Claim 8 was objected to for use of "Cph2," which was alleged to have been not previously defined. Applicants respectfully point out that Cph2 in Claim 8 is the given name of the sequence type present in SEQ ID NO:2, *see*, page 40 where Cph2 is identified as SEQ ID NO:2 and of SEQ ID NO:9 (Cph2 locus SLL0821 and Cph2-N197 respectively). Thus, Applicants submit that Cph2 is clearly defined as being the description of the sequence given.

Because the amendment and comments herein overcome the objections to the claims in the current Office Action, Applicants respectfully request that such objections be withdrawn.

Rejections to the Claims based upon 35 U.S.C. §112

Enablement

Claims 1-32 were rejected in the current Office Action under 35 U.S.C. § 112 first paragraph as allegedly lacking in enablement for compositions comprising apoproteins other than SEQ ID NO:9 (e.g., for those apoproteins comprising between about 190 and about 400 amino acids). Applicants respectfully traverse.

The Office Action sets forth a number of allegations concerning lack of enablement. For example, in alleging that the specification, "does not reasonably provide enablement for a[n] apoprotein comprising between about 190 and about 400 amino acids," the Action argues that

> the specification lacks any description of a structure of a representative number of polypeptides encoding a representative number of polypeptides sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed. Office Action at page 2 and 3.

Also, the Action alleges that, "the specification fails to teach what the critical amino acid[s] are and still achieve [a] the claimed polypeptide." Office Action at page 3.

The criteria for enablement is set out in M.P.E.P. § 2164 *et seq*. Such sections explain that,

> [t]he test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. M.P.E.P. § 2164, quoting *In re Buchner* 18 USPQ 2d 1331, 1332 (Fed. Cir. 1991).

Numerous factors can be considered in analyzing such criteria, e.g., the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, the quantity of experimentation needed to make or use the invention based on the content of the disclosure, etc. *See*, M.P.E.P. § 2164.01(a). Thus, many factors can be examined in determining whether enablement exists.

Furthermore, the conclusion of nonenablement must be based on the evidence as a whole. M.P.E.P. § 2164.01(a) citing *In re Wands* 8 USPQ 2d 1400, 1407. For example, the "presence of only one working example should never be the sole reason for rejecting claims as being broader than the enabling disclosure." M.P.E.P. § 2164.02. Also, "for a claimed genus, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled in the art . . . would expect the claimed genus could be used in that manner without undue experimentation." M.P.E.P. § 2164.02. The test for "undue experimentation," is defined by the M.P.E.P., quoting *In re Wands* at 1404, as follows:

> [t]he test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.

Based upon such criteria, Applicants respectfully hold that the claims as given are indeed enabled by the specification as filed and that no undue experimentation is required. Such enablement is replete throughout the specification as filed. For example, the specification clearly defines what comprises an apoprotein (i.e., an apoprotein as in Claim 1, etc. comprising about 190 to about 400 amino acids). *See*, e.g., page 7, line 14 through page 8, line 15 and page 17, line 1 through page 18, line 9. Such language clearly gives definitions of apoproteins, sources of apoproteins, lengths of apoproteins, domains of apoproteins, location of lyase activity in

apoproteins (i.e., in N-terminal region), methods and locations for isolation of such apoproteins, and numerous references on such apoproteins. These described apoproteins, thus, comprise examples of apoproteins amenable to use for Claim 1, etc. The specification clearly gives indication that the lyase activity in apoproteins is within the N-terminal region, thus, the about 190 to about 400 amino acid apoprotein in the claims (e.g., Claim 1, Claim 17, etc.) comprises apoproteins with those areas comprising the lyase activity. In other words, the specification describes/defines apoproteins (some of various length), of those apoprotein examples, regions of about 190 to about 400 amino acids comprising the region of lyase activity (within the N-terminal region) are easily seen. It is those lyase comprising regions (i.e., of about 190 to about 400 amino acids) that, thus, comprise the apoproteins of the claims.

Additionally, examples of apoproteins in the claims are given in the sequences listed, including not only SEQ ID NO:9, but SEQ IS NOs: 1-8 also. Thus, the language in Claim 1, Claim 17, etc. describing an about 190 to about 400 amino acid apoprotein comprising lyase activity encompasses the sequences given. Again, this is because the 190-400 amino acid apoprotein (comprising lyase activity) are subsets of the listed sequences, i.e., comprising just the about 190 to about 400 amino acid region.

Yet more enablement is shown through the specification's disclosure of commonly known methods for finding other apoproteins. For example, page 9 lines 13-19, describes common methods of sequence alignment and the like which are used to identify apoproteins (e.g., using sequences such as that in SEQ ID NO:9, etc.). Such identified apoproteins also fall within the claims since a lyase comprising region of about 190 to about 400 amino acids is easily read within the N-terminal region of them. *See*, above. Identification methods disclosed at page 10 line 22 through page 11 line 2 comprising hybridization, etc. are used in a similar manner.

Once again, while it is clear that apoproteins listed, identified, mutated, etc. are not necessarily only 196 amino acids long, like, e.g., SEQ ID NO:9, such apoproteins comprise regions of about 190 to about 400 amino acids which comprise lyase activity (found within the N-terminal region of such apoproteins). The apoproteins comprising that about 190 to about 400 amino acid length thus are found within the specification and provide the enablement of the claims.

Because the specification as filed enables the claims for apoproteins comprising between about 190 to about 400 amino acids with a lyase activity, Applicants respectfully request withdrawal of the rejection.

Written Description

Claims 1-32 were rejected in the current Office Action as lacking in written description, 35 U.S.C. § 112 first paragraph for allegedly not describing an apoprotein polypeptide of between about 190 and about 400 amino acids or a method of detection of the presence of a biomolecule using an apoprotein of between about 190 and about 400 amino acids. Applicants respectfully traverse.

The Written Description requirement is found in 35 U.S.C. § 112, first paragraph, and states:

> The specification shall contain a written description of the invention and of the manner and process of making and using it, in such full, clear concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same[.]

Additional guidance in examination of Written Description issues is found, e.g., in *Fiers v. Revel* 25 U.S.P.Q. 2d 1601. *Fiers* requires that a written description contain "a precise definition, such as by structure, formula, chemical name, or physical properties." *Fiers* at 1606. Yet further guidance is found within the USPTO's Revised Interim Written Description Guidelines Training Materials. Factors listed therein to be considered include: all disclosed distinguishing identifying characteristics (e.g., partial structure, physical and/or chemical properties, functional characteristics, known or disclosed correlation between structure and function, method of making, and combinations thereof). Such factors are to be weighed in view of the level of skill and the knowledge in the art and in light of the written description. Also of consideration is whether a representative number of species is implicitly or explicitly disclosed. A representative number of species "depends on whether one of skill in the art would recognize that applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed or claimed."

Using such criteria, Applicants submit that the specification does in fact provide the proper written description for the claimed subject matter. Again, as laid out above, the specification gives a description of the apoprotein polypeptides by listing such identifying characteristics (e.g., functional, physical, etc.) as: definitions of apoproteins, sources of apoproteins, lengths of apoproteins, domains of apoproteins, location of lyase activity in apoproteins (i.e., in N-terminal region), methods and locations for isolation of such apoproteins, and numerous references on such apoproteins. *See*, e.g., page 7, line 14 through page 8, line 15 and page 17, line 1 through page 18, line 9. These described apoproteins, thus, comprise representative examples of apoproteins amenable to use for Claim 1, etc. The specification clearly gives indication that the lyase activity in apoproteins is within the N-terminal region, thus, the about 190 to about 400 amino acid apoprotein in the claims (e.g., Claim 1, Claim 17, etc.) comprises apoproteins with those areas comprising the lyase activity. Also, the specification describes/defines apoproteins (some of various length). Within those apoprotein examples, regions of about 190 to about 400 amino acids comprising the region of lyase activity (within the N-terminal region) are seen. It is those described lyase comprising regions (i.e., of about 190 to about 400 amino acids) that, thus, comprise the apoproteins of the claims.

Other representative examples are given written description through the listed sequences (e.g., SEQ ID NO:1 through SEQ ID NO:9). It is to be noted once again, that while such sequences may, in full, be longer that about 190 to about 400 amino acids in length, the written description in the application makes clear that the apoproteins within the claims are drawn to the regions within such sequences comprising the lyase activity (in the N-terminus region) and comprising about 190 to about 400 amino acids in length.

Thus, one skilled in the art would recognize from such descriptions that Applicants possessed apoprotein polypeptides of about 190 to about 400 amino acids comprising lyase activity. Applicants therefore respectfully request that such rejection be withdrawn.

Rejections to the Claims based upon 35 U.S.C. §102(b)

Claims 1-3, 6-7, 9-22, 25 and 27-32 were rejected under 35 U.S.C. §102(b) as being anticipated by Lagarias et al., WO 98/05944. Applicants note that the present application claims priority to the U.S. parent of WO 98/05944 (i.e., USSN 60/023,217). A request for Corrected

Filing Receipt showing the proper priority is filed herewith. Accordingly, WO 98/05944 is not prior art under 35 U.S.C. § 102(b). The rejection must be withdrawn.

Rejections to the Claims based upon 35 U.S.C. §102(e)

Claims 1-3, 6-7, 9-22, 25 and 27-32 were also rejected in the current Office Action under 35 U.S.C. §102(e) as being anticipated by Lagarias et al., U.S. Patent No. 6,046,014. Applicants again note that the present application claims priority to the application which issued as U.S. Patent 6,046,014 as well as to its parental provisional application. A request for corrected Filing Receipt showing priority is filed herewith. Applicants also note that the named inventor in the current application is the sole inventor of the pertinent claimed subject matter involved in the current 102(e) rejection. Accordingly, U.S. Patent 6,046,014 is not prior art under 35 U.S.C. § 102(e) and, thus, the rejection should be withdrawn.

CONCLUSION

The current Amendments present no new matter. Applicants believe that the amendments to the claims and specification herein overcome the rejections and objections presented in the Office Action and respectfully request that such rejections and objections be withdrawn.

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

In the event that any issues of substance are perceived to remain, Applicants request that the Examiner contact the undersigned at 510-337-7871 to arrange for a telephonic interview, prior to preparation of any additional Office Action.

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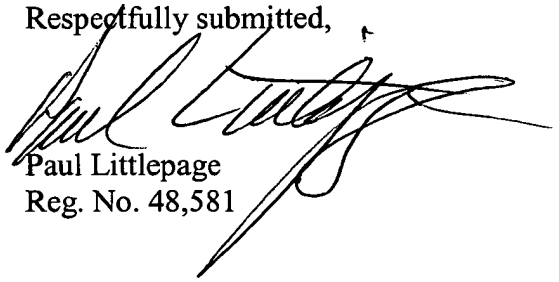
Respectfully submitted,



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APPENDIX A

"MARKED UP" CLAIMS ILLUSTRATING THE AMENDMENTS MADE TO THE CLAIMS OF 09/272,809 WITH ENTRY OF THIS AMENDMENT

5. (TWICE AMENDED) The composition of claim 4, wherein the **apoprotein [aopprotein]**polypeptide is as shown in SEQ ID NO:9.

33. (NEW) **The composition of claim 1, wherein the apoprotein polypeptide comprises from about 350 to about 400 amino acids.**

APPENDIX C

"MARKED UP" TEXT ILLUSTRATING CHANGES MADE TO THE SPECIFICATION OF 09/272,809 WITH ENTRY OF THIS AMENDMENT

Alteration at page 1, beginning at line 1:

CROSS-REFENCE TO RELATED APPLICATIONS

This is related **and claims priority** to USSN 08/904,871, filed August 1, 1997**, now issued as U.S. Patent No. 6,046,014,** (also published as WO 98/04700), **[which is a continuation-in-part of]** **and** USSN 60/023,217, filed on August 2, 1996, both of which are incorporated herein by reference for all purposes.